PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark Office, PCT
2011 South Clark Place Room CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 19 February 2001 (19.02.01)	
International application No. PCT/EP00/05841	**Applicant's or agent's file reference** BT/B45187
International filing date (day/month/year) 23 June 2000 (23.06.00)	**Priority date** (day/month/year) 29 June 1999 (29.06.99)
Applicant COHEN, Joseph et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

13 December 2000 (13.12.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer F. Baechler

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70) 14

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
MJWD/FR/B45187		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP00/05841	23/06/2000	29/06/1999

International Patent Classification (IPC) or national classification and IPC
A61K39/39

Applicant
SMITHKLINE BEECHAM BIOLOGICALS S.A. et al.

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 10 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☒ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☒ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
13/12/2000	02.10.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Leber, T Telephone No. +49 89 2399 7195

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/05841

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-15 as originally filed

Claims, No.:

1-12 as originally filed

Drawings, sheets:

1/4-4/4 as originally filed

Sequence listing part of the description, pages:

1-2, filed with the letter of 15.09.2000

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☒ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

II. Priority

1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:

   ☐ copy of the earlier application whose priority has been claimed.

   ☐ translation of the earlier application whose priority has been claimed.

2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid.

   Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:
   see separate sheet

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application.

   ☒ claims Nos. 1-12(partly).

because:

   ☒ the said international application, or the said claims Nos. 9,12 relate to the following subject matter which does not require an international preliminary examination (*specify*):
   see separate sheet

   ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-12(partly) are so unclear that no meaningful opinion could be formed (*specify*):
   see separate sheet

☒ the claims, or said claims Nos. 1-12(partly) are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-12(partly)
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-12(partly)
Industrial applicability (IA)	Yes:	Claims	1-12(partly)
	No:	Claims	

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item I
Basis of the opinion

1. Sequence listing pages ~~1-2~~ filed with the letter of 15.09.2000 do not form part of the application (Rule 13ter.1(f) PCT).

Re Item II
Priority

1. Parts of the present patent application lack priority. This concerns claim 4 as the priority document does not disclose "3 de-O-acylated monophosphoryl lipid A", claim 8 as there is no basis for the sequences named "WD1004", "WD1005" and "WD1006" in the priority document and claim 12 as there is no basis for administering the CpG oligonucleotide followed by a malaria antigen in the priority document. The related sections in the description are missing in the priority document (e.g. page 6, line 16 - page 7, line 10; page 7, line 28 - page 8, line 16; page 9, line 2-5). The following P-documents are therefore relevant for the said aspects of the application.

   a: WO 00 23105 A (SMITHKLINE BEECHAM BIOLOG ;GARCON NATHALIE (BE)) 27 April 2000 (2000-04-27)

   b: JONES T R ET AL: 'Synthetic oligodeoxynucleotides containing CpG motifs enhance immunogenicity of a peptide malaria vaccine in Aotus monkeys' VACCINE,GB,BUTTERWORTH SCIENTIFIC. GUILDFORD, vol. 17, no. 23-24, 6 August 1999 (1999-08-06), pages 3065-3071, XP004173617 ISSN: 0264-410X

Re Item III
Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Claim 1 relates to a vaccine which encompasses a "malaria antigen" and an "immunostimulatory CpG oligonucleotide". Both expressions lack clarity and

support by the description to such an extent that a meaningful opinion can not be formed (Art 34(4)(a)(ii) PCT). The said objections also affect claims 2-12. In its present form, the product of claim 1 is defined by the result to be achieved ("antigen", "immunostimulatory") without providing technical features to define the intended scope of the invention.

2. In view of the objections raised above, examination of the claims will be restricted to the combination of the malaria antigens RTS, RTS* and TRAP as referred to in claim 2 and defined in the description and the sequences defined in claim 8 with the limitation that sequence WD1005 will not be considered. This sequence does not include all feature of the independent claim (claim 1) to which claim 8 refers, as a CpG dinucleotide is not present (Guidelines Section IV, III-3.4) and may, if maintained in the claim, result in an objection to lack of unity (Rule 13 PCT).

3. Claims 9 and 12 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Basis for the assessment of novelty, inventive step and industrial applicability

1.1 Reference is made to the following document/s/:

D1: WO 96 02555 A (UNIV IOWA RES FOUND) 1 February 1996 (1996-02-01) cited in the application

D2: WO 98 40100 A (DAVIS HEATHER L ;OTTAWA CIVIC LOEB RESEARCH INS (CA); QIAGEN GMBH) 17 September 1998 (1998-09-17)

D3: WO 98 05355 A (SMITHKLINE BEECHAM BIOLOG ;COHEN JOSEPH (BE)) 12 February 1998 (1998-02-12) cited in the application

D4: WO 99 11241 A (SMITHKLINE BEECHAM BIOLOG ;GARCON NATHALIE (BE); MOMIN PATRICIA MA) 11 March 1999 (1999-03-11)

D5: WO 00 23105 A (SMITHKLINE BEECHAM BIOLOG ;GARCON NATHALIE (BE)) 27 April 2000 (2000-04-27)

D6: JONES T R ET AL: 'Synthetic oligodeoxynucleotides containing CpG motifs enhance immunogenicity of a peptide malaria vaccine in Aotus monkeys' VACCINE,GB,BUTTERWORTH SCIENTIFIC. GUILDFORD, vol. 17, no. 23-24, 6 August 1999 (1999-08-06), pages 3065-3071, XP004173617 ISSN: 0264-410X

2. Novelty

2.1 None of the documents cited in the ISR disclose the combination of the CpG sequences WD1001-WD1004, WD1006, WD1007 and a malaria antigen RTS, RTS* or TRAP. Therefore, claims 1-12 appear to be novel (Art 33(2) PCT). The same applies to those aspects of the present application which have no valid priority.

3. Inventive step

3.1 Document D1 discloses the use of unmethylated CpG dinucleotides because of their ability to stimulate an immune response (D1, Abstract). The CpG oligonucleotides have a the basic structure of $X_1X_2CGX_3X_4$ (D1, page 7, line 16) and may encompass phosphorothioate bonds, which stabilise the molecule (page 7, lines 21-27). With the exception of WD1005 (see Item III above), each of the sequences referred to in claim 8 are specific examples of the basic structure disclosed in this document. D1, further discloses the use of CpG oligonucleotides as a vaccine adjuvant (D1, page 7, line 38) to boost the subjects immune response whereby the CpG oligonucleotide may be administered in conjunction with the vaccine or slightly before the vaccine (D1, page 21, lines 18-21).

3.2 Document D2 discloses that nucleic acids containing at least one unmethylated CpG dinucleotide affect the immune response in a subject (D2, Abstract). The CpG oligonucleotide may be 8-30 bases in size and may be stabilised through backbone modifications such as phosphorothioate bonds (D2, page 8, line 20;

page 9, lines 5-16). In particular, D2 discloses the sequence of WD1001 (D2, page 10, line 26, SEQ ID NO:3). D2 further discloses the use of CpG oligonucleotides as adjuvant, whereby the vaccine may be an antigenic polypeptide such as the hepatitis B virus surface antigen (D2, claim 15; page 19, lines 1-4). This results in a strong humoral and cellular immune response which exceeds that induced by the vaccine or the CpG oligonucleotide alone. This was further improved by the addition of aluminium ions ("alum") as adjuvant (D2, page 19, lines 4-22; page 20, lines 6-15).

3.3 Document D3 discloses a vaccine composition for the prevention or treatment of malaria (D3, Abstract). In particular D3 discloses the antigens RTS (page 2, line 25 et seq.) and TRAP (page 5, line 21). D3 further discloses the use of adjuvants such as 3 de -O-acylated monophosphoryl lipid A (D3, page 4, line 21) and saponin derived substances (page 4, lines 26-29).

3.4 Document D4 discloses a vaccine composition encompassing Malaria antigens such as RTS, RTS,S and TRAP and adjuvants (D4, page 7, lines 17-29). The adjuvants may be a metabolisable oil such as 3 De-O-acylated monophosphoryl lipid A in combination with a saponin (D4, page 2, lines 9-28). Moreover, D4 discloses that the vaccine may be adsorbed to $AlOH_3$ as adjuvant (D4, page 13, lines 16-21). Finally, D4 discloses that the vaccine may comprise further antigens such as human, bacterial or viral nucleic acid (D4, page 11, lines 21-26).

3.5 The examined part of claim 1 differs from closest prior art documents D3/D4 in that the vaccine formulation encompasses the presence of a CpG oligonucleotide as defined in claim 8. The technical problem is therefore to provide an improved vaccine formulation. The solution referred to in claim 1 is the combination of a known malaria antigen with a CpG oligonucleotide.
A person skilled in the art challenged with the problem to improve the antigenic ability of an antigen would obviously consider to modify the adjuvant. As documents D1 and D2 belong to the closely related prior art, the skilled person would turn to adjuvants with a proven adjuvant activity such as the CpG oligonucleotides disclosed in D1 and D2 (see 3.1 and 3.2 above). Thus, claim 1 lacks an inventive step (Art 33(3) PCT). This opinion is not affected by the fact that the precise sequences as disclosed in claim 8 are not disclosed in D1 or D2

as no surprising effect appears to be associated with the said oligonucleotides

3.6 Claims 2-8 appear not to encompass features which in combination with the features of claim 1 appear to fulfil the requirements of Art 33(3) PCT for inventive step.

3.7 The independent claims 9-12 lack an inventive step for the same reasons as outlined in 3.5 above.

3.8 Document D5 discloses vaccines formulations (D5, page 7, lines 1-10) encompassing a metallic salt (e.g. $AlPO_4$, $AlOH_3$; D5, page 17, Table 1), an immuno-stimulant (e.g. CpG oligonucleotides (D5, page 6, lines 28-32); a saponin derivate (D5, page 6, lines 18-27), 3 De-O-acylated monophosphoryl lipid A (D5, page 6, lines 1-13) and an antigen such as RTS,S and TRAP (D5, page 12, line 13). Similarly, document D6 discloses the vaccines combining CpG containing oligonucleotides and a synthetic peptide from the circumsporozoite protein of Plasmodium falciparum (D6, Abstract).
Thus an inventive step (Art 33(3) PCT) can not be acknowledged for claims 1-12 insofar at they do not have a valid claim to priority.

4. Industrial applicability

4.1 The subject-matter disclosed in the claims 1-8, 11 of the present application appears to be industrially applicable (Art 33(4) PCT).

4.2 For the assessment of the present claims 9, 10 and 12 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VI
Certain documents cited

1. The following documents have an earlier priority and filing date than the present application and their subject matter may therefore be of relevance for the examination of the present application in its regional or national phase.

   WO 00 62800 A (SMITHKLINE BEECHAM BIOLOG ;FRIEDE MARTIN (BE); GARCON NATHALIE (BE) 26 October 2000 (2000-10-26)

Re Item VII
Certain defects in the international application

1. To meet the requirements of Art 5 and Rule 5 PCT, the documents D1-D4 should be identified in the description and the relevant background art disclosed therein should be briefly discussed if the subject-matter for which these documents are relevant prior art remains in the claims.

Re Item VIII
Certain observations on the international application

1. Claim 2 lacks clarity (Art 6 PCT) as the meaning of RTS, RTS* and TRAP appear to be internal designations unknown to the person skilled in the art.

2. The meaning of "immunological equivalent derivates" in claims 2 and 3 is unclear and appears to lack support by the description (Art 6 PCT).

3. The terms "CpG dinucleotides" (claim 5) and "CpG oligonucleotide" (claims 6 and 7) lack clarity and support by the description (Art 6 PCT).

4. Claims 4-6, 8 and 10 refer to other claims as "claimed herein". This results in a lack of clarity (Art 6 PCT) as these claims refer to both product and method claims.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
BT/B45187		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/EP 00/ 05841	23/06/2000	29/06/1999
Applicant		
SMITHKLINE BEECHAM BIOLOGICALS S.A.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [X] furnished subsequently to this Authority in written form.

   [X] furnished subsequently to this Authority in computer readble form.

   [X] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [X] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [X] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [ ] the text is approved as submitted by the applicant.

   [X] the text has been established by this Authority to read as follows:

   USE OF CPG AS AN ADJUVANT FOR MALARIA VACCINE

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

   [ ] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [X] None of the figures.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

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4 January 2001 (04.01.2001)

PCT

(10) International Publication Number
WO 01/00231 A2

(51) International Patent Classification[7]: A61K 39/00

(21) International Application Number: PCT/EP00/05841

(22) International Filing Date: 23 June 2000 (23.06.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
9915204.3 29 June 1999 (29.06.1999) GB

(71) Applicant *(for all designated States except US)*: **SMITHKLINE BEECHAM BIOLOGICALS S.A.** [BE/BE]; Rue de L'Institut 89, B-1330 Rixensart (BE).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **COHEN, Joseph** [US/BE]; SmithKline Beecham Biologicals S.A., Rue de l'Institut 89, B-1330 Rixensart (BE). **GARCON, Nathalie** [FR/BE]; SmithKline Beecham Biologicals S.A., Rue de l'Institut 89, B-1330 Rixensart (BE). **VOSS, Gerald** [DE/BE]; SmithKline Beecham Biologicals S.A., Rue de l'Institut 89, B-1330 Rixensart (BE).

(74) Agent: **TYRRELL, Arthur, William, Russell**; SmithKline Beecham, Corporate Intellectual Property, Two New Horizons Court, Brentford, Middlesex TW8 9EP (GB).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *Without international search report and to be republished upon receipt of that report.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 01/00231 A2

(54) Title: VACCINES

(57) Abstract: A vaccine formulation for the prevention or amelioration of plasmodium infection in humans is provided. The vaccine comprises a malaria antigen, especially a protein which comprises a portion of the CS protein of P. falciparum fused in frame via a linear linker to the N-terminal of HBsAg, and an immunostimulatory CpG oligonucleotide. Methods for making the vaccine formulation of the invention are described. Patients may also be treated by pre-administration of the CpG oligonucleotide prior to administration of the malaria antigen.

INTERNATIONAL SEARCH REPORT

Interr nal Application No
PCT/EP 00/05841

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K39/39 A61P33/06 //(A61K39/39,39:005)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
BIOSIS, MEDLINE, SCISEARCH, EMBASE, CHEM ABS Data, WPI Data, EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 98 05355 A (SMITHKLINE BEECHAM BIOLOG ;COHEN JOSEPH (BE)) 12 February 1998 (1998-02-12) cited in the application the whole document	1-12
Y	WO 99 11241 A (SMITHKLINE BEECHAM BIOLOG ;GARCON NATHALIE (BE); MOMIN PATRICIA MA) 11 March 1999 (1999-03-11) the whole document	1-12
Y	WO 96 02555 A (UNIV IOWA RES FOUND) 1 February 1996 (1996-02-01) cited in the application abstract claims 1,5,10,18	1-12

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
19 January 2001	26/01/2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl. Fax: (+31-70) 340-3016	Niemann, F

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/EP 00/05841

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	WO 98 40100 A (DAVIS HEATHER L ;OTTAWA CIVIC LOEB RESEARCH INS (CA); QIAGEN GMBH) 17 September 1998 (1998-09-17) abstract; claim 16	8
A	WO 98 37919 A (UNIV IOWA RES FOUND) 3 September 1998 (1998-09-03) abstract page 27, line 20	8
P,X	WO 00 23105 A (SMITHKLINE BEECHAM BIOLOG ;GARCON NATHALIE (BE)) 27 April 2000 (2000-04-27) abstract; claims 1-26	1-7,9-12
E	WO 00 62800 A (SMITHKLINE BEECHAM BIOLOG ;FRIEDE MARTIN (BE); GARCON NATHALIE (BE) 26 October 2000 (2000-10-26) abstract page 15, line 12 - line 30 claims 1-10	1-12
P,X	JONES T R ET AL: "Synthetic oligodeoxynucleotides containing CpG motifs enhance immunogenicity of a peptide malaria vaccine in Aotus monkeys" VACCINE,GB,BUTTERWORTH SCIENTIFIC. GUILDFORD, vol. 17, no. 23-24, 6 August 1999 (1999-08-06), pages 3065-3071, XP004173617 ISSN: 0264-410X the whole document	1-12

INTERNATIONAL SEARCH REPORT

.ormation on patent family members

Inter nal Application No
PCT/EP 00/05841

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9805355 A	12-02-1998	AU 706303 B	10-06-1999
		AU 4204097 A	25-02-1998
		BG 103141 A	31-08-1999
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